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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,502	09/18/2001	Diana Downs	960296.97559	9804

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/955,502	DOWNS ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 16-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 16-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-18-05 has been entered.

The amendment and declaration filed 4-18-05 has been entered into the record. Claims 2-15 have been cancelled. Claims 1 and 16-26 are pending and under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

The rejection of claims 1, 7 and 8 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn based on amendment to the claims.

The rejection of claims 1 and 7 under 35 U.S.C. 102(b) as being anticipated by Pianzzola et al (Journal of Bacteriology 178(23):6736-6742, 1996 is maintained for reasons made of record for claims 1, 2, 3 and 7 in the Office action mailed 12-22-03 is withdrawn based on the amendments to the claims.

Rejections Maintained

Claim 1 and 16-26 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons made of record for claims 1-

8 in the Office action mailed 12-22-03. It is noted for the record that the two rejections made for separate claim sets have now been combined into one rejection set forth in its totality herein for simplification of the record. Each of the issues are identified and the corresponding relevant claims identified.

As to claims 1, 16, 17 and 18, Applicants' arguments and amendment has been carefully considered, but the claims still recites "gene". This issue can be resolved by amending the claim to recite "comprising the step of vector-based expression of a nucleic acid encoding the YggX polypeptide as set forth in SEQ ID NO:11".

As to all the claims (1 and 16-26) Applicants argue that that the claimed invention should not be limited to vector-based over expression of the endogenous YggX gene and submit a Declaration by Diana Downs. Declarant Downs attest that heterologous bacterial expression systems are well known and widely accepted in the art of bacteriology. This is not persuasive, Declarant uses may publications that do not establish the state of the art at the time of the invention. Declarant indicates that the declaration established that overexpression of heterologous YggX proteins provides for cells more resistant to superoxide damage. To support this position, Declarant indicates that it is routine in the art to express a wide variety of heterologous polypeptide in *E. coli*. This is not the issue, the issue is whether the expression of any heterologous YggX protein provides for the same phenotype (i.e. reducing superoxide damage or increasing resistance of an eubacterial enzyme). Declarant recognized this specific problem in paragraph 2 of the declaration. The fact that heterologous proteins can be expressed in *E. coli* does not provide written description of possession of the phenotypic effect of the heterologous protein expression now claimed in the genus of eubacterium. The art does not document that the YggX proteins as described herein are interchangeable using conventional complementation analysis as argued in paragraph 5 of the declaration. Declarant further establishes at paragraph 4 that vector based expression systems are widely practiced. This is in fact true, but claims 19-26 are not so limited. At paragraph 5, Declarant attests that the

publications illustrate the value of heterologous expression to define function by *in vivo* complementation. Declarant again does not attest to the state of the art at the time of filing. Further, this specification does not use complementation to demonstrate that even one of the asserted yggX homolog function as claimed in any heterologous background. The later publications establish functional complementation for specific genes and not for the claimed genus of yggX proteins. This specification does not establish functional complementation for any yggX gene in any heterologous system. None of the homologs were characterized with respect to function in any heterologus system. The specification as filed and the declaration does not establish possession by way of written description of functional complementation of yggX homologs in the genus of eubacteria as claimed. It is not clear that they can complement in fact each other. The publications cited by Declarant establish functional interchangeability of other genes using standard complementation tests. Again, these tests are not performed in this application or by Declarant. Characterization is not performed in a heterologous host or using SEQ ID NO:11 over-expression in any other eubacterial cell such as the ubiquitous "tractable" *E. coli* upon which Declarant relies. Declarant has not established that the newly described yggX protein family or homologs are interchangeable (i.e. complement each other). Applicants specification is apparently devoid of the similar teachings of the art that are required to establish and define functional similarity for this newly described genus and function of the yggX protein. The specification merely invites one to further testing. The declaration fails because there is no extrinsic evidence presented that a heterologous yggX protein functionally complements a described microorganism with a known functional defect or in fact is heterologously expressed and displays the claimed function. The declaration merely presents the classical experimentation needed to determine functional equivalence. This specification as filed lacks this intrinsic evidence of written description for possession of the claimed genus and the Declaration does not provide any extrinsic evidence using the classical methodology of the art relied upon by Declarant Downs to

establish functional equivalence of the claimed genus. Declarant further attests that the application itself establishes a mixing and matching of yggX gene at pages [0029] - [0036]. This is not persuasive, these passages apparently indicates that the yggX gene was apparently obtained from *S. enterica* was and the yggX gene from *S. enterica* was used for vector-based over-expression in *S. enterica*. This passage does not apparently demonstrate heterologous expression and "mixing and matching" of functional equivalents as asserted by Declarant. Declarant indicates that [0025] indicates that while we have performed experiments thus far in bacterial cells we anticipate similar mechanisms of protection to occur with yggX in other cell types, including yeast, mammalian and plant cells. This is not persuasive, as it directly contradicts Applicants admission that at the time the invention was made no yggX sequences were apparent in ay archeal or eukaryotic genome sequence available in GeneBank Databases at NCBI. Therefore, passage [0025] is mere speculation especially in view that the specification goes on to admit that no archeal or eukaryotic equivalents of yggX protein were to be found one of the largest databases in the world. Further, the specification explicitly teaches "The phenotypes characterized herein were the result of relatively high levels of YggX." [0060] and the only means presented herein for such expression is vector-based overexpression of endogenous YggX protein to achieve those high levels of endogenous YggX protein. Therefore the Declaration is not persuasive to obviate the rejection under 112 1st paragraph since the specification as filed does not provide a correlation of particular structure with the claimed function for the genus of YggX proteins and functional equivalence in heterologous systems. There is no known correlation of structure with function in the art and the specification does not provide intrinsic evidence of a correlation of structure with function for heterologous expression or any functional complementation.

As to claims 17, 18, 23, 24 and 25 Applicants arguments have been carefully considered but are still not persuasive. Applicants argue that the claims are drawn to particular YggX homologs particularly disclosed. This is not persuasive. The claims are not

drawn to the particularly disclosed homologs of SEQ ID NOS:2-33. The specification defines homologs as variants with a function substantially identical to the *Salmonella typhimurium* YggX protein with at least 45% and preferably 55% amino acid identity. As such, the claims read on unlimited variations of the disclosed YggX proteins of SEQ ID NOS:2-33 that have "substantially identical function" that is not defined in the claim or in the specification. As such, the YggX family having a substantially identical function to the *Salmonella typhimurium* is set forth in the claims by way of structure and function. As previously set forth recitation of "YggX" does not convey a common structure or function, nor does the recitation of "obtained from" since the endogenous gene is not defined by structure and function. The scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members are permitted. Structural features that could distinguish compounds in the "YggX" genus from others in the protein class are missing from the disclosure and the claims. The "obtained from" language used in the claim does not define any particular structure and reads on variants obtained therefrom which have no written description in the specification as filed.

The rejection is maintained.

Claims 1, 16, 17, 18, 19, 21, 23 and 25 stand under 35 U.S.C. 102(b) as being anticipated by Gralnick et al (Abstracts of the General meeting of the American Society for Microbiology, 100p441, May 21-25, 2000 is maintained for reasons made of record for claims 1, 7 and 8.

Applicants declaration has been considered, but is moot. A declaration cannot obviate a rejection under 102(b). Priority has not been granted to the provisional document for reasons made of record.

New Rejections

Claims 1 and 16-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained essentially for reasons made of record in the final rejection mailed 10-18-04 and reasons made of record herein. This is a new matter rejection.

The claims have been amended to recite "wherein the lack of increase in superoxide dismutase activity is relative to cells not expressing the yggX gene" or 'wherein the increased resistance is relative to cells not expressing the YggX protein/homolog". These recitations have no apparent written support in the specification as originally filed. The basis for comparison of activity as claimed is relative to "any cell" not expressing the yggX gene/homolog. This is not supported by the specification as filed. The sole apparent support for this language is at [0058], "We observed no increased superoxide dismutase activity in *yggX** mutant extracts," and the basis for comparison is not explicitly stated in the specification and is not stated relative to vector-based expression or co-expression or if this was observed in the genus. The yggX* mutant is not apparently generated using a vector-mediated expression system. It is unknown how the yggX* mutant was generated and what it was specifically compared to and the answer does not logically flow from the recited passage. There are at least two possibilities the *Salmonella typhimurium* wild type strain DM5104, or DM5647 where the yggX was disrupted (see page 5-6, description of Figure 2). There is no indication of which of these two, if either, was used for the comparison. Further, the basis for comparison as recited in the claims is *any cell*, which includes eukaryotes, that do not express the YggX protein and the passage simply does not conceptually support this amendment. With respect to increased resistance relative to cells not expressing the yggX protein/homolog, this language has no implicitly or explicit support in the specification as filed. This issue is best resolved by Applicants pointing to

the specification by page and line number where written description support can be found for these limitations.

As to claims 19-26, the claims recite the genus of "an eubacterial enzyme". The specification neither identifies such enzymes or their nucleic acids. While the specificaiton teaches obtaining yggX nucleic acids from several microorganisms and eubacterial cells in particular, the specification does not provide conception by way of written description of the genus of eubacterial enzymes. An eubacterium as defined in by the art is a genus of gram-positive, rod-shaped bacteria found in cavities of man and animals and plant products, infections of soft tissue and soil. Some species may be pathogenic and no endospores are produced (see On-Line Medical Dictionary definition). The specification does not contemplate this genus of enzymes with labile Fe-S cluster/centers, the description of a Fe-S cluster is limited to aconitase in *E. coli*, a bacterium that is not a eubacterium and does not fall within that genus. The specificaiton as filed therefore does not contemplate the subgenus of enzymes as recited in the claims. This issue is best resolved by Applicants pointing to the specification by page and line number where specific written description support can be found for this new subgenus.

Claims 1 and 16-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 1 and 16-26, the term 'eubacteria" is *prima facie* indefinte because it use in the specification and the claims is inconsistent with any known definition. The specificaiton uses the term "eubacteria" consistently. The specification does not define this term. It is important to note that the term is never capitalized as is proper and conventional with terms designating orders, families and subdivisions of taxonomic classification. The art defines ""Eubacteriales", "Eubacteria" and eubacterium (singular form of eubacteria) specifically. Eubacteriales is an obaolete name for an order of

bacteria including gream negative, gram positive sporeforming and non-sporeforming species. The art defines Eubacteria as a subdivision of the prokaryotes and includes all except Archaebacteria, most gram-positive bacteria, cyanobacteria, mycoplasmas, enterobacteria, pseumonads and chloroplasts. The art defines a eubacterium as a genus of gram-positive rod-sphaped bacteria bacteria found in cavities of man and animals and plant products, infections of soft tissue and soil. Some species may be pathogenic and no endospores are produced (see definitions from the On-line Medical Dictionary). The specification discuses at page 14 that there are 23 eubacteria [0047]. It is clear from the definition of "Eubacteria" that there are more than 23 eubacteria. As such, the term is used in the specification in a manner inconsistent with the definition of "Eubacteria". Further, use of the term "eubacteria" is inconsistent with defination of the singular term "eubacterium" as set forth in the art. The term is not defined in the specification as filed. Since "eubacterium' is inconsistent with "Eubacteria" and the specification never capitalizes the term and uses it in a manner inconsistent with the scope of "Eubacteria" the metes and bounds of the term cannot be asceratined by the skilled artisan.

As to claim 1, the claim recites ".. vector-based expression of "a" YggX gene (SEQ ID NO:11)". The recitation of "a" means any and it is not clear if the sequence presented in parenthesis is intended to limit the gene. The same issue is apparent in claims 19 and 20. The listing of a sequence identifier in parenthesis is confusing because it is not clear that the YggX protein is limited to that particular sequence.

As to claims 18, 23 and 25, the recitation of 0157H7EDL933, 0157_H7, CT18 are indefinite because they do not define a proper genus and species of bacteria. Furthermore, many of the genus and species of bacteria are incomplete (i.e. A. actin., S. para, K. pneumo, N. meningitA, N. meningitB) and it is unclear what genus and species are specifically being referenced. Applicants are specifically cautioned against adding new matter to add additional description.

As to claim 21, the term "the YggX protein" lacks antecedent basis in the claim.

Claims 1, 16, 17, 18, 19, 21, 23 and 25 stand under 35 U.S.C. 102(b) as being anticipated by Gifford et al (Journal of Bacteriology, 181(14):4223-4236, July 1999).

Gifford et al teach incubation of *E. coli* in standard media. Gifford et al teach that the native mutY and yggX genes are co-transcribed and Applicants admitt at page 14 [0047] that the genes are co-transcribed in *E. coli*. As such, the 'incubation" provides for co-expressing as claimed. MutY protein is an enzyme that contains a labile Fe-S cluster as admitted by Applicant at paragraph [0056]. As such, the incubation of *E. coli* inherently provides for the claimed method. The yggX protein of the prior art is inherently SEQ ID NO:11. The recitation of co-transcription does not distinguish the method of the prior art from the instantly claimed invention.

Status of Claims

Claims 1 and 16-26 stand rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to

reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy
Primary Examiner
Art Unit 1645